

## **I. Remarks**

Applicants submit these amendments with a Request for Continued Examination in view of the Advisory Action mailed January 7, 2008, in which the Examiner stated that entry of the after final amendments filed November 16, 2007, would present new grounds for search and consideration. Applicants previously filed an Amendment and Notice of Appeal on November 16, 2007, in response to a final Office Action dated June 20, 2007. Applicants respectfully request entry of these amendments and that the previously-filed amendments dated November 16, 2007, not be entered.

Claims 1, 5-17, 19-24, 31-36, 40-52, 54-59 and 67-74 are pending. Claims 1, 5-8, 24, 31, 35, 36, 40-43, 59, 67-69 and 74 have been amended herein to more clearly define the invention. Claims 2, 4, 18, 37, 39 and 53 have been cancelled herein without prejudice or disclaimer of the subject matter claimed therein. No issues of new matter should arise and entry of these amendments is respectfully requested.

## **II. Enablement**

Claims 1, 2, 4-24, 31-37, 39-59, and 67-74 remain rejected under 35 USC 112, first paragraph, for allegedly lacking enablement for 1) a transgenic fish whose genome comprises any oncogene operably linked to any promoter wherein the oncogene is not expressed and does not cause T-cell lymphoblastic leukemia or 2) a method of using said fish as broadly claimed. Applicants respectfully traverse this rejection.

The claims as amended are directed to transgenic fish whose genome comprises an oncogene operably linked to a lymphoid-specific promoter, wherein the oncogene is expressed in lymphoid cells and induces leukemia or lymphoma. Support for this amendment can be found, throughout the specification, for example, on page 19, line 2, page 20, line 28 to page 21, lines 1-6, page 22, line 11, page 30, lines 9-15, page 39, lines 4-5, page 41, line 23, page 48, lines 15 and 24-26, page 49, lines 11-14 and 28-29, page 50, line 6, page 51, line 29, page 54, line 20 and page 55, lines 6-11.

Applicants have shown at least two working examples of the claimed transgenic fish. In example 1, Applicants have shown transgenic fish expressing the T-cell oncogene cMYC, operably linked to the lymphoid-specific Rag2 promoter, wherein the oncogene induced T-cell acute lymphoblastic leukemia or lymphoma. In example 2, Applicants have shown transgenic fish expressing the B-cell oncogene BCL2, operably linked to the Rag2 promoter, wherein the oncogene induced an anti-apoptotic phenotype that occurs in B-cell transformation such as that seen in follicular B-cell lymphoma.

Contrary to the Examiner's assertion that the specification does not provide the guidance necessary to make a transgenic fish expressing any oncogene other than cMYC operably linked to a Rag2 promoter, Applicants respectfully submit that the person of ordinary skill who understood and appreciated the teachings of the specification would recognize that lymphoid-specific promoters in fish that could express a B- or T-cell oncogenes in lymphoid cells, at levels sufficient to result in leukemia or lymphoma, other than the specifically disclosed cMYC operably linked to Rag2 embodiment, was possible as of the filing date without undue experimentation.

With respect to the method claims, the claims have been amended to recite the comparison step "comparing the leukemia or lymphoma in said transgenic fish after contact or exposure to said test drug or agent relative to the leukemia or lymphoma of said fish prior to contact or exposure with said test drug or agent; wherein suppression of the leukemia or lymphoma in said transgenic fish after contact or exposure to said test drug or agent relative to the leukemia or lymphoma of said fish prior to contact or exposure with said test drug or agent is indicative of a test drug or agent that suppresses oncogene-induced leukemia or lymphoma" to more clearly define the claimed invention.

Support for this amendment can be found, throughout the specification, for example, on page 31, lines 19 and 24, page 33, line 20, page 34, line 9, page 46, line 26, page 54, line 27 and page 63, lines 11-13. Applicants respectfully submit that the person of ordinary skill would not need to look beyond the lymphoma or leukemic phenotype of the transgenic fish prior to treatment as a means of comparison to the treated fish itself to

determine whether the test drug or agent suppresses the oncogene-induced lymphoma or leukemic phenotype.

In view of the foregoing, Applicants respectfully submit that the claims as amended are fully enabled by the application. Withdrawal of this rejection is respectfully requested.

### **III. Written Description**

Claims 18 and 53 remain rejected under 35 USC 112 as allegedly failing to comply with the written description requirement. The Examiner asserts that the specification has not described an oncogene substantially similar to cMYC in terms of its structural or functional identity. Applicants respectfully traverse this rejection.

However, in order to advance prosecution of this application, claims 18 and 53 have been cancelled herein without prejudice or disclaimer of the subject matter claimed therein.

Accordingly, Applicants respectfully submit that this 112 rejection is rendered moot with reference to cancelled claims 18 and 53.

### **IV. New Matter**

a. Claims 1, 2, 4-24 and 26-35 are newly rejected under 35 USC 112, first paragraph as allegedly failing to comply with the written description requirement.

As discussed above, the claims as amended are directed to transgenic fish whose genome comprises an oncogene operably linked to a lymphoid-specific promoter, wherein the oncogene is expressed in lymphoid cells and induces leukemia or lymphoma. The specification as originally filed discloses support for this recitation, for example, in examples 1 and 2, such that one of skill in the art would understand the metes and bounds of the claims. In view thereof, withdrawal of this rejection is respectfully requested.

b. Claims 36-37, 39-59 and 67-74 are newly rejected under 35 USC 112, first paragraph as allegedly failing to comply with the written description requirement.

As discussed above, the claims as amended are directed to a method of screening test drugs or agents that suppress oncogene-induced leukemia or lymphoma. The specification as originally filed discloses support for this recitation, for example, in examples 1 and 2, such that one of skill in the art would understand the metes and bounds of the claims. In view thereof, withdrawal of this rejection is respectfully requested.

#### **V. Indefiniteness**

Claims 18 and 53 remain rejected under 35 USC 112, second paragraph as allegedly being indefinite. Applicants respectfully traverse this rejection.

However, in order to advance prosecution of this application, claims 18 and 53 have been cancelled herein without prejudice or disclaimer of the subject matter claimed therein.

Accordingly, Applicants respectfully submit that this 112, second paragraph rejection is rendered moot with reference to cancelled claims 18 and 53.

#### **VI. Authorization**

The Commissioner is authorized to charge the two-month extension of time fee in the amount of \$230.00 to Deposit Account No. 08-0219, in addition to the \$405.00 fee for the accompanying Request for Continued Examination.

The Commissioner is also authorized to charge any other fees necessary to maintain the pendency of the present application or to credit any overpayments to Deposit Account No. 08-0219, under Order No. 0112706.00123US2 from which the undersigned is authorized to draw.

## **VII. Conclusion**

An early and favorable reconsideration and allowance of the pending claims is respectfully requested. If the Examiner believes that any further discussion of this communication would be helpful, she is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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